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## FK-506 (FK506,Tacrolimus, Fujimycin) [F10:

**Alternative Product ID:** Tacrolimus, Fujimycin

**Description:** FK506 is an immunosuppressant that blocks T cell proliferation in vitro the generation of several lymphokines, especially IL-2. Shown to inhibit the activity of binding protein and inhibit the Ca2+-dependent phosphatase and calcineurin.

**Chemical Formula:** C44H69NO12

**Molecular Weight:** M.W. 804.0

**Solubility:** FK506 is soluble in DMSO and MeOH. Suggested stock concentration in 10mM.

**CAS Number:** CAS [104987-11-3]

**Active Product:** Y

**Appearance:** Off-White Solid

**Purity:** >98%

**Handling:** Store in Tightly Sealed Vial.

**Storage:** +4 C.

**Shipping:** Express Courier

**Bulk Quantity:** Inquire

**$110.00**

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Xiao-Dong and Amy, Preclinical Biology



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# Press Release

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**Study Of ABX-CBL In Steroid Resistant Graft Versus Host Disease Does Not Meet Primai**

Fremont, CA - February 18, 2003 - SangStat Medical Corporation (Nasdaq: SANG) and Abge ABGX) disclosed today that Phase II/III study results indicate ABX-CBL demonstrated a surviv days in patients with acute steroid-resistant graft vs. host disease (GVHD) that was similar to A Thymocyte globulin, equine, Pharmacia), the study's control arm. ABX-CBL is a murine monoclonal antibody in co-development by Abgenix and SangStat. The study was designed to superior survival with ABX-CBL, and, therefore, did not meet its primary endpoint. The comp plan further development of ABX-CBL.

"The ABX-CBL study results are unambiguous, and SangStat intends to focus its current effort marrow transplant arena on Thymoglobulin," said Richard D. Murdock, Interim Chairman, P CEO at SangStat. "While we are disappointed that the results were not favorable, turning off t program will allow SangStat to channel all our resources toward our internal development progi

"ABX-CBL was an in-licensed murine antibody which was being developed for a small approximately 2,000 patients per year in the United States who contract steroid-resistant G\ was not expected to make a large contribution to the future profitability of Abgenix, the disappointed that this patient group will not be receiving a therapeutic benefit," said Raymond president and chief executive officer of Abgenix. "We will continue to focus our clinical efforts c our lead cancer product candidate, and on building our integrated fully human antibod development and manufacturing business."

SangStat reiterates its financial guidance for 2003 of $0.35 - $0.45 EPS. SangStat intends tc resources earmarked for ABX-CBL toward the ongoing development of Thymoglobulin® (an globulin), the Company's successful rabbit polyclonal antibody.

SangStat

SangStat is a global biotechnology company focused on immunology and working to discover, market high value therapeutic products in the autoimmune, hematology/oncology and immun areas. SangStat's U.S. headquarters are in Fremont, California. SangStat also maintai international presence, including direct sales and marketing forces in Canada, France, Ge Spain, and the UK, and distributors throughout the rest of the world. SangStat's stock is t Nasdaq under the symbol "SANG." The company's web site is located at www.sangstat.com.

Abgenix

Abgenix is a biopharmaceutical company focused on the development and commercializati therapeutic antibodies. The company's technology platform, which includes XenoMouse® a (TM) technologies, enables the rapid generation and selection of high affinity, fully human anti

candidates to a variety of disease targets. Abgenix leverages its leadership position in hur technology by building a diversified product portfolio through the development of its own intern products and through the establishment of licensing arrangements with multiple ph biotechnology and genomics companies. For more information on Abgenix, visit the company www.abgenix.com.

Statements made in this press release about Abgenix' technologies, product developme collaborative arrangements and manufacturing activities, other than statements of historical fa its projected financial results, are forward-looking statements and are subject to a number of that could cause actual results to differ materially from the statements made, including risks as the success of clinical trials, the progress of research and product development progra manufacturing, the regulatory approval process, competitive products, future capital requirem extent and breadth of Abgenix' patent portfolio. Please see Abgenix' public filings with the S Exchange Commission for information about risks that may affect Abgenix.

This press release contains forward-looking statements that involve risks and uncertainties. Fo statements reflect SangStat's current views with respect to future events. Forward-lookin include plans for the development of ABX-CBL and Thymoglobulin, as well as SangStat's fin for 2003. Actual results may vary materially and adversely from those anticipated, believed, otherwise indicated. Factors that could cause actual results to differ materially include, with progress and results of the Thymoglobulin studies; market conditions or other developments competitors; increased sales or price reductions by competitors; reduction in margin on k reduction in demand or failure of demand to reach anticipated levels; manufacturing matters delays; increases in expenses; changes in reimbursement for products; patent and other litiga results from the pending Gengraf litigation; licensing or product transactions; delays in enrollment; complications or delays in conducting pre- clinical or clinical trials; requests from t agencies for additional clinical trials; or changes in management. For a discussion of the factors that might result in different outcomes, see "Risk Factors" in SangStat's 2001 Annu Form 10-K, its 2002 quarterly reports on Form 10-Q and other documents filed with the S Exchange Commission. SangStat assumes no obligation to update any such forward-lookin risks or reasons why actual results might differ.

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NATIONAL MARROW DONOR PROGRAM®

**Improved Management of Graft-Versus-Host Disease**

The development of new drugs to treat graft-versus-host disease (GVHD), combined with early detection and advances in understanding the underlying mechanisms of the disease, have resulted in significant reductions in the morbidity and mortality of this potential complication of allogeneic transplantation.

As a result of these advances, the risk of grade II-IV acute GVHD after allogeneic related transplants has decreased from 45% in 1976 to under 30% in 2001. [1] Importantly, the majority of this decrease has been in the most severe manifestations (grades III-IV).

By definition, GVHD is classified as acute if it occurs before day 100 post-transplant and chronic if it persists or develops beyond day 100. Successful strategies to treat each type of GVHD have been developed.

## Prevention of Acute GVHD

Several successful strategies are used to reduce the risk of developing acute GVHD. These include:

- Prophylaxis with immunosuppressive drugs
- Selective depletion of alloreactive T lymphocytes from the donor graft
- Using umbilical cord blood as the source of donor cells
- Using more precise HLA-matched donors

**Prophylaxis with immunosuppressive drugs.**
Intensive prophylaxis with immunosuppressive drugs is standard practice for all patients undergoing allogeneic transplantation. Standard drugs in use include cyclosporine, methotrexate, several types of corticosteroids and antithymocyte globulin. The decrease in the incidence and severity of acute GVHD cited above is in large part due to the widespread prophylactic use of these drugs, particularly cyclosporine and methotrexate. See Advances in Conditioning Regimens for more information.

**Selective depletion of alloreactive T lymphocytes from the donor graft.**
GVHD is a manifestation of alloreactive donor T cells acting against the patient. Deleting donor T cells prior to infusion into the patient is an effective method of reducing the risk of developing GVHD. However, doing so raises the risk of graft failure, infection and relapse. In addition, T cell depletion can reduce the beneficial graft-versus-malignancy effect that can act to eradicate residual disease in the patient. However, newer techniques to selectively deplete only alloactivated donor T cells from donor grafts have produced promising results. [2]

**Using umbilical cord blood as the source of donor cells.**
Because of the immunological immaturity of the T cells in umbilical cord blood, transplants using this source of cells have a reduced incidence and severity of GVHD. [3,4] Although more commonly used in pediatric patients, cord blood transplantation has been successfully used in adults when sufficient nucleated cell doses are used. [4] See Hematopoietic Cell Sources Tailored to the Patient for more information.

**More precise HLA matching between donor and patient.**
The phasing out of serological tissue typing and its replacement with DNA-based tissue typing has increased the accuracy and specificity of HLA typing, which allows for more precise HLA matching between donors and transplant patients. Because the alloreaction of donor T cells against the patient's cells is reduced as the degree of HLA match is increased, more precise HLA matching can significantly reduce both types of GVHD. [5]

## Treatment of Acute GVHD

If acute GVHD does develop after transplantation, glucocorticoids such as methylprednisolone or

prednisone in combination with cyclosporine are administered. Satisfactory responses to this steroid treatment are observed in 50% to 75% of patients. New drugs and new strategies are available now or are in clinical trials that can supplement standard treatment, including:

- Monoclonal antibodies (e.g., anti-CD3, -CD5, and -IL-2 antibodies)
- Mycophenolate mofetil
- Alemtuzumab (Campath)
- Antithymocyte globulin (rabbit ATG)
- FK506
- Sirolimus [6]

**Chronic GVHD**
Primary therapy for chronic GVHD is administration of steroids, usually cyclosporine and prednisone on alternating days. Clinical trials investigating treatments of steroid-refractory chronic GVHD using the following drugs have reported success rates of between 25% and 50%:

- Tacrolimus
- Mycophenolate mofetil
- Thalidomide
- Daclizumab
- Extracorporeal photopheresis
- Infliximab
- Clofazimine [7]

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